42. (New) The composition of claim 40, wherein said neurodegenerative disorder is selected from the group consisting of degeneration of cells in the spinal cord, physical deterioration, death of spinal cord cells, abnormal pattern of spinal cord cells, spinal cord injury, amyotrophic lateral sclerosis, multiple sclerosis, syringomyelia, spinal tumors or metastasis, and spinal cord infections (e.g., parasitic or bacterial infections).

43. (New) The method of claim 36, wherein said spinal cord injury is selected from the group consisting of compression, contusion, distraction, and solid core lesion.

44. (New) The method of claim 37, wherein said neurodegenerative disorder is selected from the group consisting of degeneration of cells in the spinal cord, physical deterioration, death of spinal cord cells, abnormal pattern of spinal cord cells, spinal cord injury, amyotrophic lateral sclerosis, multiple sclerosis, syringomyelia, spinal tumors or metastasis, and spinal cord infections (e.g., parasitic or bacterial infections). --

REMARKS

Objection To The Drawings

The Examiner indicates that the formal drawings are objected to for reasons stated in the PTO Form 948 Notice of Draftsperson's Patent Drawing Review. Applicant notes the objections to the drawings raised by the draftsperson. Corrected formal drawings, in compliance with 37 C.F.R. §1.48(p), will be submitted upon indication of allowable subject matter.

Objection To The Specification

The Examiner notes several minor typographical errors in the specification. Accordingly, this amendment corrects all typographical errors noted by the Examiner and responds in full to this objection.

Claim Amendments

Claims 1, 8, 10, 18, 25, 26, and 36 are amended to more particularly and distinctly claim the subject matter which Applicant regards as the invention and to address the issues raised by the Examiner under 35 U.S.C. §112. Claims 9 and 27 are canceled without prejudice herein. New claims 39-44 are added. Accordingly, claims 1-8, 10-26, and 28-44 are pending in the application. Support for new claims 39-44 can be found in the specification and/or claims as filed and/or previously pending. No new matter has been added. The amendments and addition of the claims are made solely for the purpose of expediting prosecution. They are not to be construed as an acquiescence to any rejections, and Applicant reserves the right to further prosecute the same or similar claims to those as originally filed in this or another application.

Claim Rejections – 35 U.S.C. §112

35 U.S.C. §112, First Paragraph

Claims 1-38 are rejected under 35 U.S.C. §112, first paragraph, because, according to the Examiner, the specification "*does not reasonably provide enablement for any and all xenographic subjects, any and all types of spinal cord damage or injury, any and all antigens, any and all cell surface antigen alterations, any and all treatments, any and all molecules, and any and all neurodegenerative disorders.*" Applicant respectfully traverses this rejection for at least the following reasons.

The pending claims pertain to compositions and methods for the delivery of spinal cord cells for the transplantation into a mammalian xenogeneic subject comprising an isolated spinal cord cell obtained from a pig, such that treatment of spinal cord damage is obtained upon transplantation into the subject.

With respect to xenogeneic subjects, the specification teaches that the spinal cord cells of the invention can be administered to any xenogeneic subject. In addition, Applicant has presented working examples of the use of claimed compositions and methods in two different art-recognized animal models using two different species of hosts. It is Applicants position that one of ordinary skill in the art could select any host of a different species than a pig for transplantation. However, in the interest of expediting

prosecution of the application, claims 1 and 18 are amended to specify "mammalian" xenogeneic subjects. Support for these amendments are found, for example, on page 16, lines 14-21. Accordingly, it is Applicant's position that the claims comply with the requirements of §112, first paragraph.

With respect to various types of damage, injury, or disorders suitable for treatment using the claimed compositions and methods, Applicant asserts that the invention teaches for a variety of different types of deficits that would benefit from transplantation of spinal cord cells. First, Applicants point out that the claims require a specific result, i.e., that treatment be obtained upon administration of the subject compositions. Accordingly, the claims only embrace conditions that are suitable for treatment. Moreover, the specification teaches numerous specific spinal cord deficits suitable for treatment using the claimed compositions and methods, including: supplementation of damaged spinal cord cells in a host with new cells for spinal cord injury, including, compression, contusions, distraction, and solid core lesions, neurodegnerative disorders, including, degeneration of cells in the spinal cord, physical deterioration, death of spinal cord cells, abnormal pattern of spinal cord cells, spinal cord injury, amyotrophic lateral sclerosis, multiple sclerosis, syringomyelia, spinal tumors or metastasis, and spinal cord infections (e.g., parasitic or bacterial infections), and aging (*see* for example, page 15, lines 13-33 of the specification). It is Applicant's position that one of ordinary skill in the art would be able to identify candidate disorders for treatment without undue experimentation, particularly given the working Examples presented in the specification. Applicants provide working examples of spinal cord transplantation using two art-recognized models. Applicants maintain that it would not require undue experimentation for one of ordinary skill in the art to determine whether to treat a given spinal cord deficit using the claimed compositions or methods.

Moreover, under 35 U.S.C. §112, first paragraph, the Examiner has the "initial burden of setting forth a reasonable explanation as to why the scope of protection provided by [claims 1-38] is not adequately enabled by the description of the invention provided in the specification." *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993). Specifically, in *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995), it was held that:

> *Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.*

Additionally, the court stated that in the absence of a reason to doubt the objective truth of the teachings contained in the specification, the methods of making and using the claimed invention must be taken as complying with the requirements of §112, first paragraph. The Examiner has not met this burden.

Claims 8-11 and 25-30 are rejected because the Examiner states that these claims, as written, read on any and all antigens where the specification fails to provide any teachings or guidance with regard to any type of antigen other than an MHC class I antigen. Applicant traverses this rejection on the grounds that the teachings of the specification enable one of ordinary skill in the art to modify other antigens (such as adhesion molecules, e.g., NCAM-1 or ICAM-1). However, in the interest of expediting prosecution, claims 8 and 25 have been amended to recite that the antigen on the cell surface is an MHC class I antigen. Claims 9 and 27 are canceled. The remaining claims 10-11 and 26, 28-30 are dependent from 8 and 25, respectively. Therefore, this rejection is believed to be obviated.

With respect to the means of alteration of antigens, the Examiner contends that the claims read on any and all molecules and that the specification is only enabling for $F(ab')_2$ fragment of a monoclonal antibody PT85. Applicants point out that the specification teaches a variety of agents that can be used to alter cell surface antigens, including non-complement fixing polyclonal or monoclonal antibodies, or fragments thereof (e.g., $F(ab')_2$ fragments), or peptides. Applicants also point out that the antigen on the cell surface which is to be modified has been limited to the MHC class I antigen. Accordingly, applicants submit that the claims meet the requirements of §112, first paragraph.

In light of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of these 35 U.S.C. §112, first paragraph, rejections.

35 U.S.C. §112, Second Paragraph

Claims 26-30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite and for lack of clarity for the recitation of "which is capable of stimulating an immune response." This rejection is believed to have been obviated by the amendment to claim 26. Claim 26, from which claims 28-30 depend, has been amended to clarify that the term "antigen" modifies the phrase "capable of stimulating an immune response." Support for this amendment may be found, for example, on page 2, lines 25-27, and on page 6, lines 3-4. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

Claim Rejections – 35 U.S.C. §102(e)

Claims 1, 2, 5-7, 13-16, 18, 19, 22-24, and 31-38 are rejected under 35 U.S.C. §102(e) as being anticipated by Gage et al., U.S. Patent No. 5,762,926 (1998) (Pat. No. '926). The Examiner indicates that "*Gage et al. teach the composition and method of transplantation of embryonic neuronal cells and glial cells (including astrocytes and oligodendrocytes), as both a homogenous population of cells, or as a mixture, into the spinal cord of a mammalian (including human) subject, to facilitate reconnection or ameliorative interactions of injured and damaged neurons (including those resulting from a neurodegenerative disorder such as amyotrophic lateral sclerosis) in the spinal cord (i.e. to treat spinal cord damage).*" The Examiner proposes that Gage et al. meet the claim limitations of the present application.

Applicant respectfully traverses this rejection. For a prior art reference to anticipate a claimed invention under 35 U.S.C. §102, the prior art must teach each and every element of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

The present invention pertains to compositions and method of treating spinal cord damage in a xenogeneic subject using ***porcine spinal cord cells***.

In contrast, Gage et al. use donor cells, such as, fibroblasts, glial cells, adrenal cells, hippocampal cells, keratinocytes, hepatocytes, connective tissue cells, ependymal cells, bone marrow cells, stem cells, leukocytes, chromaffin cells and other mammalian cells. *See* Pat. No. '926, column 13, lines 39-45. Specifically, Gage et al. teach the use of rat fibroblast cells using grafting techniques (*see* Example 1, column 23, line 42). Gage et al. also uses a method of grafting such donor cells that are genetically modified using vectors to transport transgenes selected from the group consisting of tryptophan hydroxylase, GABA-decarboxylase, enkephalin, dopa decarboxylase (AADC), ciliary neuronal trophic factor (CNTF), brain derived neurotrophic factor (BDNF), neurotrophin (NT)-3, NT-4, and basic fibroblast growth factor (bFGF). Gage et al. does not anticipate the pending claims since the reference fails to teach each and every element of the claimed invention. Specifically, Gage fails to teach or suggest the use of porcine spinal cord cells as required by independent claims 1 and 18. The remaining claims depend from claims 1 and 18 and add additional limitations that are patentable over the cited art. Because Gage et al. fails to disclose the use of porcine spinal cord cells, Applicant respectfully requests this 35 U.S.C. §102(e) rejection be reconsidered and withdrawn.

Claim Rejections – 35 U.S.C. §103(a)

Claims 3, 4, 8-12, 17, 20, 21 and 25-30 are rejected under 35 U.S.C. §103(a) as being unpatentable over Fraser et al., PCT WO96/14398 (1996), further in view of Gage et al. (1998). The Examiner states that Fraser et al. "*teach a composition for transplantation into a xenogeneic subject to treat neurodegneration in the brain, comprising an isolated cortical cell, mesencephalic cell or striatal cell, obtained from a pig*" while Gage et al. "*teach a method of treating donor cells so as to minimize or reduce graft rejection.*" The Examiner, in particular, alleges that there is motivation to combine the references to make the claimed invention obvious. Applicant respectfully traverses this rejection.

To establish a *prima facie* case of obviousness for the claimed invention, there must have been some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the

reference or to combine reference teachings in the manner proposed by the Examiner. Second, there must have been a reasonable expectation of success at the time the invention was made. ***Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.*** See M.P.E.P. 2143. The prior art must suggest "to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process" and "[b]oth the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Dow Chemical Co.* 837 F.2d 469. 473, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

While Fraser et al. teach the use of porcine mesencephalic cells for the treatment of neurodegenerative diseases in a xenogeneic subject, they fail "to teach the use of porcine spinal cord cells to treat spinal cord injury or degeneration in their disclosed composition or method of treatment," as admitted by the Examiner. The secondary reference cited by the Examiner, Gage et al., also fail to teach or suggest the use of porcine spinal cord cells in the treatment of spinal cord damage. As set forth above, the reference discloses the use of many cell types, but fails to teach or suggest the use of porcine spinal cord cells as required by the claims.

Thus, it is Applicant's position that neither of the cited references teach or suggest the use of porcine spinal cord cells as required by the pending claims. Since the cited references do not teach or suggest all the elements of the claims, the claims are not obvious over the references. Accordingly, applicants respectfully request that the rejection of claims 3, 4, 8-12, 17, 20, 21, and 25-30 be reconsidered and withdrawn.

CONCLUSION

In view of the above amendments and remarks, it is believed that the present application is in condition for allowance.

If a telephone conversation with Applicant's Agent would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicant's Agent at (617) 227-7400.

Respectfully submitted,

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